Wisconsin Department of Health and Family Services

Pharmacy NewsCapsule

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Antipsychotics and Dementia

By Doug Englebert, Pharmacy Practice Consultant

The Food and Drug Administration (FDA) has released the following public health advisory:

The FDA has determined that the treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality. Fifteen out of the total seventeen placebo-controlled trials performed with **olanzapine** (Zyprexa), **aripiprazole** (Abilify), **risperidone** (Risperdal), or **quetiapine** (Seroquel) in elderly demented patients with behavioral disorders showed numerical increases in mortality in the drug-treated group as compared to the placebo-treated patients. A total of 5,106 patients were enrolled in these studies, and several analyses demonstrate an approximately 1.6-1.7 fold increase in mortality. Examination of the specific causes of these deaths revealed that most were either due to heart related events (e.g., heart failure, sudden death) or infections (mostly pneumonia).

The atypical antipsychotics fall into three drug classes based on their chemical structure. Because the increase in mortality was seen with atypical antipsychotic medications in all three chemical classes, the FDA has concluded that the effect is probably related to the common pharmacologic effects of all atypical antipsychotic medications, including those that have not been systematically studied in the dementia population. In addition to the drugs that were studied, the atypical antipsychotic medications include **clozapine** (Clozaril) and **ziprasidone** (Geodon). All of the atypical antipsychotics are approved for the treatment of schizophrenia; however, none are approved for the treatment of behavioral disorders in patients with dementia. Because of these findings, the FDA will ask the manufacturers of these drugs to include a Boxed Warning in their labeling describing this risk and noting that these drugs are not approved for this indication. **Symbyax**, a combination product containing olanzapine and fluoxetine, approved for the treatment of depressive episodes associated with bipolar disorder, will also be included in the request.

The FDA is also considering adding a similar warning to the labeling for older antipsychotic medications because the limited data available suggest a similar increase in mortality for these drugs.

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Inside This Issue

USP 797 and Home Health

By Doug Englebert, R.Ph.

A few months ago, information on the United States Pharmacopoeia (USP) 797, the new standard for sterile compounding, was introduced at a BQA Home Health Advisory Meeting. A reminder: USP is a standard-setting body that, in some cases, creates standards that become enforceable by agencies like the Food and Drug Administration and the Joint Commission of Accreditation of Health Care Organizations.

In January of 2004, USP unveiled a new standard for sterile compounding that is referred to as USP 797.

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New Drugs

By Doug Englebert, R.Ph.

New Products		
Byetta	Exenatide	An injectable agent to improve blood sugar control in type 2 diabetes.
Symlin	Pramilintide	An injectable agent to be used in combination with insulin to improve postprandial blood glucose control in type 1 and 2 diabetes
Mycamine	Micafungin	Antifungal for prevention and treatment of Candida infections.
New Forms or Uses		
Boniva	Ibandronate	Once a month oral bisphosphonate for osteoporosis
Fosamax Plus D	Alendronate/cholecalciferol	Osteoporosis, plus Vitamin D
Niravam	Alprazolam	Dissolving tablet for anxiety and panic disorder
Xibrom	Bromfenac	Anti-inflammatory eye drop
Bextra	Valdecoxib	WITHDRAWN
Tysabri	Nataluzimab	SUSPENDED

Medication Errors

Doug Englebert, Pharmacy Practice Consultant

What's on the Medication Administration Record?

How is the order written or typed on the medication administration record (MAR)? This is a critical question. If the order is open to confusion, errors may occur.

For example, sometimes a medication requires two tablets to make up the dose. Dosage errors have occurred when the MAR is written as follows: **Amaryl 4mg (2 tablets) once a day.** The order is confusing; do you give two 4 mg tablets or two 2 mg tablets?

To avoid dosage errors write the order as follows: **Amaryl 4 mg (Give two 2 mg tablets for a total of 4 mgs) each day.**

Focus Drug of the Month

By Doug Englebert, R.Ph

Lunesta™ (eszopiclone)

Lunesta™ is a schedule IV controlled nonbenzodiazepine hypnotic agent indicated for the treatment of insomnia. In controlled outpatient and sleep laboratory studies, Lunesta™ administered at bedtime decreased sleep latency and improved sleep maintenance.

Lunesta™ comes in a 1 mg, 2 mg or 3 mg tablet. The typical non-elderly adult dose is 2 mg taken immediately before bed. The dose can be increased to 3 mg. For elderly adults with complaints about falling asleep, the dose is 1 mg tablet taken immediately before bed. The dose can be increased to 2 mg if necessary. Elderly adults whose complaints are difficulty staying asleep are advised to take 2 mg tablets immediately before bed. Significant side effects include unpleasant taste, dizziness, confusion, and somnolence.

Lunesta™ information for patients indicates that extended use of Lunesta™ should be discussed with their physician. Patient information provided by the manufacturer recommends that the medication be taken immediately prior to bed and should not be taken with a large high-fat meal.

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BQA has received questions about whether the FDA advisory changes the survey process or regulations. To address these questions, BQA will issue a memo indicating that regulations and survey process have not changed. Long term care surveyors have been directed for some time by Centers for Medicare and Medicaid Services to review antipsychotic medications used for behaviors related to dementia. The standard of practice prior to using antipsychotics for behaviors in dementia is to ensure: the behavior is not from some other medical, environmental, or social need or condition; the behavior is persistent; and the behavior is harmful. If these conditions are met, antipsychotic medications may need to be used. After discussion with residents, providers should weigh the benefits and risks and decide what is best for the resident.

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Sterile compounding is basically mixing two or more medications together to produce a sterile product. This may include taking injectable vitamins and adding them to a total parental nutrition intravenous (IV) bag, or before taking a vial of antibiotic, reconstituting and mixing it with a normal saline IV solution. There are other more complex examples of compounding as well.

The USP standard creates classes of sterile products (low, medium and high risk). Each of these classes of products requires a specific sterile environment in which to compound. In addition, the beyond-use-dates (expiration dates) are limited based on the class of the product.

Home health agencies (HHAs) that are JCAHO accredited, federally certified, or state licensed should be aware of medication standards related to sterile compounding, and should work to meet those standards to maintain JCAHO requirements. HHAs should work with their pharmacy to ensure the "field" compounding that agency staff perform in the homes of patients meets the USP standards and JCAHO requirements. Typically, field compounding may be allowed when the medication is used immediately. However, if the sterile medication is prepared and stored for use at a later date, the USP standards and manufacturer requirements may limit how long that medication can be stored and used.

The patient information also warns patients not to take Lunesta™ unless they are able to sleep for eight hours.

Lunesta™ has been studied in elderly individuals. However, as is the case for most new medications, now that it is approved and used more frequently, potential adverse effects may surface.

In the elderly there are some concerns to consider with Lunesta™. Elderly individuals need to be aware of altered taste which may contribute to weight loss. Another concern includes day after drowsiness which may lead to increased falls or declines in activities of daily living. They may be more sensitive to changes in cognition or may be more likely to experience behavioral changes related to Lunesta™ use similar to what may occur with other sleep medications.

In nursing homes, surveyors look at hypnotics when used for greater than ten consecutive days. Although Lunesta™ has been used effectively for up to six months, surveyors should look at Lunesta™ use lasting more than ten continuous days. There is still a need to evaluate if the resident has had an assessment related to sleep loss, and if the use of the medication has been effective.

If there are medications you would like featured in this column, please send an email to Doug at **engleda@dhfs.state.wi.us**

Consultant's Corner

Doug Englebert *Pharmacy Practice Consultant PRQI*

This section will appear in each issue and will contain information that will answer your questions. If there is a topic about which you want more detailed information, please drop me an email at **engleda@dhfs.state.wi.us** and I'll research the topic.

1. **An update on situational use antipsychotics and benzodiazepines.**

In the Oct/Nov/Dec 2004 issue, situational use of haloperidol and benzodiazepines was discussed. The information is still current and should be reviewed. However, expanding on that discussion, situational use medications are often used at bathing times. The reason for drug use is that behavior interventions have been tried and failed and that a bath must be provided for the patient. However, have all behavior interventions been tried? A great resource to address behaviors at bathing is a video/CD ROM called Bathing Without a Battle. This resource provides many practical interventions for bathing that can be used to avoid the use of medications.

2. **Can staff at a nursing home, assisted living facility, hospice, home health agency, etc., split tablets to meet the dose of medication ordered by the physician?**

In general, there are no specific regulations that state "Thou shall not split tablets." However, there are regulations that require medications to be packaged in unit dose or unit of use, which means the medication needs to be packaged in a way that the final dose needed to meet the physician order is separately packaged. In addition, some regulations prohibit transfer of the medication to another package by anyone other than a physician or a pharmacist. Therefore, if a nurse splits a tablet and gives a half tablet now, placing the other half tablet in a package to be used later, the action may constitute a violation of regulations.

Regulations aside, is splitting of tablets at the point of administration a good idea? In some cases, medications may not be available in the dose needed and there is no choice but to split a tablet. In other cases, there may be substantial cost savings in using split tablets. These can be legitimate reasons for splitting tablets.

There are studies that show degrees in variability in the final dose when tablets are split. The variability in dose for each half tablet depends on the medication, the device being used to split the tablets, and the person who splits tablets. For some medications, the variability between split tablets will not have a significant clinical impact. In other cases, the variability in dose can have a significant impact and splitting tablets should be avoided.

Recently a question was posed asking if Warfarin could be split. The reason was that the patient was having lab draws twice a week and dose changes occurred at the same frequency. Splitting tablets allowed staff not to have to maintain so many different strengths of Warfarin in the facility. The issue to consider is whether the patient is already apparently unstable on Warfarin. Splitting tablets may increase that instability. Warfarin is not produced to be split. In fact, there are many strengths of warfarin available, so that this practice can be avoided. **Therefore, although the regulations may allow splitting for this instance, actually splitting tablets may not be in the best interest of the patient.**

References are available upon request.